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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,093	09/30/2002	Josef Altenbuchner		7125

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EXAMINER	
RAMIREZ, DELIA M	
ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,093	ALTENBUCHNER ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *2-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/21/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 1-8 are pending.

Applicant's election with traverse of Group I, claims 1, 6- 8 drawn to a hydantoin racemase from A. aurescens DSM3747, and a method of use of said racemase, in a communication filed on 12/20/2004 is acknowledged.

Applicant's traverse is on the ground(s) that according to Annex B, Example 17, there is unity of invention between a protein and its coding DNA. Applicants submit that Groups I-II would also have unity of invention since Group I is directed to a protein, and Group II is directed to a DNA encoding said protein, vectors and microorganisms containing the DNA.

Applicant's arguments have been fully considered but are not deemed persuasive to withdraw the restriction requirement. The Examiner acknowledges Example 17 and agrees that the protein and the DNA exhibit a corresponding technical feature. However, as previously indicated, according to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. In the instant case, the special technical feature is not a contribution over the prior art in view of the fact that Pietzsch et al. teach the hydantoin racemase from A. aurescens DSM 3747. Thus, lack of unity exists between Group I and II.

The requirement is deemed proper and therefore is made FINAL.

Claims 2-5 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1, 6-8 are under consideration and are being examined herein.

Specification

1. The abstract of the specification is objected to due to the recitation of "gene encoding for the racemase....and microorganisms comprising this gene are to be protected. Use in a process for the

production of ...." for the following reasons. The language of the abstract should be in the narrative form, clear and concise, and should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details. In the instant case, the term "are to be protected" is unclear since one cannot determine the meaning of this term within the context of what is being described. Furthermore, the term "use in a process ..or derivatives thereof" does not provide the reader with an indication as to what is being used in the process recited. Appropriate correction is required.

2. The specification is objected for not complying with sequence rules. Applicant is required to insert sequence identifiers in front of sequences referred to in the specification using the required format, i.e. " SEQ ID NO: #". See, particularly 37 CFR 1.821(d). For example, in page 2, line 27, "(Seq. 4)" should read "(SEQ ID NO: 4)". Applicant is requested to make the appropriate changes.

3. The disclosure is objected to because it lacks a Brief Description of the Drawings section. See MPEP § 608.01(f). Appropriate correction is required.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: Isolated hydantoin racemase from A. aurescens DSM 3747.

Priority

5. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. 119(a)-(d) to EUROPEAN PATENT OFFICE (EPO) 99118956.4 filed on 09/27/1999. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The contents of the foreign document are in English.

6. This application is the US national stage of PCT/EP00/08580 filed on 09/02/2000.

Information Disclosure Statement

7. The information disclosure statement (IDS) submitted on 3/21/2002 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Objections

8. Claim 1 is objected to due to the recitation of "rec-hydantoin racemase...". For consistency with commonly used claim language, it is suggested that the claim be amended to recite "A....racemase....". Appropriate correction is required.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 1, 6-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 1, as written, does not sufficiently distinguish over proteins as they exist naturally because the claim does not particularly point out any non-naturally occurring differences between the claimed product and the naturally occurring products. In the absence of the hand of man, the naturally occurring product is considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 US 303, 206 USPQ 193 (1980). The claim should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified" as taught in page 10, lines 4-21, of the specification. See MPEP 2105. Claims 6-8 are directed to a use, which is non-statutory subject matter, i.e. a product or a process. For examination purposes, it will be assumed that claims 6-8 are directed to a process of use of the hydantoin racemase of claim 1.

11. Claims 6-8 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112, Second Paragraph

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claims 6-8 as interpreted provide for the use of the hydantoin racemase of claim 1, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

15. Claim 7 (claim 8 dependent thereon as interpreted is indefinite in the recitation of "use according to claim 6 in a process for the production of enantiomerically enriched compounds" as it is unclear how the instant claim further limits claim 6 as interpreted. As indicated above, claim 6 has been interpreted as being directed to a process for the production of amino carboxylic acids with the hydantoin racemase of claim 1. Claim 7 as written, while depending upon claim 6, appears to be directed to a separate process for the production of enantiomerically enriched compounds. For examination purposes, it will be assumed that the claim is directed to a process according to claim 6 wherein the amino carboxylic acids are enantiomerically enriched amino carboxylic acids". Correction is required.

16. Claim 8 is indefinite in the recitation of "use according to claim 6 and/or 7" as it is unclear how one can have a process according to both claim 6 and 7. Also, it is noted that the instant claim is an improper multiple dependent claim as a multiple dependent claim must be in the alternative only. For examination purposes, it will be assumed that the term "and/or" reads "or". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

18. Claims 1, 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to a genus of hydantoin racemases from A. aurescens DSM 3747. While the specification discloses the structure of one hydantoin racemase from A. aurescens (SEQ ID NO: 4), the specification is silent in regard to the structure of other hydantoin racemases from A. aurescens DSM 3747 or the critical structural elements in the polypeptide of SEQ ID NO: 4 which are required in any hydantoin racemase from A. aurescens DSM 3747. While a sufficient written description of a genus of proteins may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus, in the instant case, there is no structural feature recited. Thus, potentially structurally unrelated polypeptides are encompassed by these claims. It is noted that Wiese et al. (J. Biotechnol. 80:217-230, 2000; cited in the International Search Report) teaches that it is possible that more than one hydantoin racemase can be found in A. aurescens DSM 3747 (page

226, right column, Discussion, first paragraph). Claims 6-8 as interpreted are directed in part to a process for the production of a genus of enantiomerically enriched amino carboxylic acids, or derivatives thereof, with the hydantoinase racemase of claim 1. While the specification teaches that the hydantoinase racemase of SEQ ID NO: 4 can racemize BH, and to a lesser extent, MTEH and IMH (Table 2), the specification is silent in regard to other enantiomerically enriched amino carboxylic acids which can be produced with said racemase. Since the art teaches that there are differences in substrate specificities among hydantoin racemases, one of skill in the art would not expect to use the hydantoin racemase of SEQ ID NO: 4 for the production of any enantiomerically enriched amino carboxylic acid. The specification only discloses a single hydantoin racemase from A. aurescens and a few species of the genus of compounds which can be racemized with the polypeptide of SEQ ID NO: 4, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of the claimed invention. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

19. Claims 1, 6-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ a novel bacterial strain. Since this bacterial strain is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the strain. The specification does not disclose a repeatable process to obtain the strain and it is not apparent if the strain is readily available to the public. Accordingly, it is deemed that a deposit of this strain should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that Applicants have deposited the strain but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be available to the public under the conditions specified in 37 CFR 1.808, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

a. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;
b. upon granting of the patent the strain will be available to the public under the conditions specified in 37 CFR 1.808;
3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
d. the deposit will be replaced if it should ever become unviable.

20. Claims 1, 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 4, and a method to produce enantiomerically enriched 5-benzyl-hydantoin (BH), 5-(3'-indolylmethylene)-hydantoin (IMH) and 5-(2'-methylthioethyl)-hydantoin (MTEH) does not reasonably provide enablement for (1) any hydantoin racemase from A. aurescens DSM 3747, (2) a method for the production of any enantiomerically enriched amino carboxylic acid, or derivative thereof, with (1) or the polypeptide of SEQ ID NO: 4, or (3) a method for the production of any amino carboxylic acid, or derivative thereof, with (1) or the polypeptide of SEQ ID NO: 4.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the large number of unknown amino carboxylic acids and hydantoin racemases of unknown structure encompassed by the claims. As indicated above, while the specification provides the structure and functional characterization of the polypeptide of SEQ ID NO: 4, the specification is silent in regard to (a) the structures of other hydantoin racemases from A. aurescens DSM 3747, (b) the structural elements in the polypeptide of SEQ ID NO: 4 which should be present in any hydantoin racemase from A. aurescens DSM 3747, and (c) other substrates which can be used to produce any enantiomerically enriched amino carboxylic acid with the polypeptide of SEQ ID NO: 4 or any hydantoin racemase from A. aurescens DSM 3747.

While the argument can be made that one could use the structure of the polypeptide of SEQ ID NO: 4 and isolate other hydantoin racemases via structural homology, the art teaches the unpredictability of determining function based solely on structural homology and discloses examples of how small structural differences can result in major differences in enzymatic activity. Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β–ketoacyl synthase into a malonyl decarboxylase and completely eliminates β–ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Since structure determines function, one of skill in the art would require some knowledge or guidance as to how structure correlates with the desired

function. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to display the desired enzymatic function, and the unpredictability of the prior art in regard to function based on structural homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to (1) isolate those polypeptides having hydantoin racemase activity as encompassed by the claims, and (2) determine which substrates can be used to produce any enantiomerically enriched amino carboxylic acid with the polypeptide of SEQ ID NO: 4 or any hydantoin racemase from A. aurescens DSM 3747.. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 1, 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Pietzsch et al. (DECHEMA Biotechnology Conferences 4:259-262, 1990; cited in the International Search Report of PCT/EP00/08580).

Claim 1 is directed to a hydantoin racemase from A. aurescens DSM 3747. Claims 6-7 as interpreted (see Claim Rejections under 35 USC 112, second paragraph for claim interpretation), are directed in part to a method to produce enantiomerically enriched amino carboxylic acids with a hydantoin racemase from A. aurescens DSM 3747. Pietzsch et al. teaches the isolation and characterization of a hydantoin racemase from A. aurescens DSM 3747 (page 260, last sentence, Table 1; Purification procedure). Pietzsch et al. also teaches the enzymatic racemization of 5-IMH (Figure 1, page

259), therefore teaching a method for the production of enantiomerically enriched amino carboxylic acids. As such, the teachings of Pietzsch et al. anticipate the instant claims as written.

Claim Rejections - 35 USC § 103

22. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

23. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

24. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pietzsch et al. (DECHEMA Biotechnology Conferences 4:259-262, 1990; cited in the International Search Report of PCT/EP00/08580) in view of Bommarius et al. (Chirality in Industry, Chapter 20, pages 371-397, 1992; cited in the International Search Report). The teachings of Pietzsch et al. have been discussed above. Pietzsch et al. does not teach an enzyme-membrane reactor. Bommarius et al. teaches the use of membrane-enzyme reactors for the production of enantiomerically pure α-amino acids and the use of hydantoin racemases in such reactors (Figure 1, pages 373, 384-385, 387). Bommarius et al. does not teach a hydantoin racemase from A. aurescens DSM 3747.

Claim 8 as interpreted is directed to a method to produce enantiomerically enriched amino carboxylic acids with a hydantoin racemase from A. aurescens DSM 3747 in an enzyme-membrane reactor.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use an enzyme-membrane reactor, as taught by Bommarius et al., in the method of Pietzsch et al. A person of ordinary skill in the art is motivated to use an enzyme-membrane reactor in the method of Pietzsch et al. because enzyme-membrane reactors allow reuse of the enzyme while preserving their activity, therefore reducing the high cost associated with separation of the enzyme from products and/or reactants (page 373, first paragraph). One of ordinary skill in the art has a reasonable expectation of success at using an enzyme-membrane reactor in the process of Pietzsch et al. since Bommarius et al. teaches the use of enzyme-membrane reactors with hydantoin racemases. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Art of Interest

25. It is noted that Wiese et al. (J. Biotechnol. 80:217-230, 2000; cited in the International Search Report) discloses the heterologous expression, isolation and characterization of a hydantoin racemase from A. aurescens DSM 3747. Wiese et al. also teaches using the enzyme for the production of enantiomerically enriched amino carboxylic acids.

Conclusion

26. No claim is in condition for allowance.

27. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (571) 273-8300. The faxing of such papers must conform with the

notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

28. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
March 10, 2005

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600